Appendix A

Model summary under the Bayes1 prior

Fixed effect model	Random effect model (homogeneous)	Random effect model (heterogeneous)	Random effect model (inconsistency)
Data $r_{ik} \sim Bin(n_{ik}, p_{ik})$ i = 1, …, NS; k = 1, …, NT (NS = number of study; NT = number of trt) **Model** $logit(p_{ik}) = \mu_i + d_k$ where $\mu_i$is the log odds of baseline treatment and d_k is the fixed effect of the k^{th} drug versus the placebo **Prior** $d_k \sim N(0, 10000)$ $\mu_i \sim N(0, 10000)$	**Data** $r_{ik} \sim Bin(n_{ik}, p_{ik})$ **Model** $logit(p_{ik}) = \mu_i + \delta_{ik}$ where δ_{ik} is the random effect of the k^{th} drug versus the placebo in theith study **Prior** $\delta_{ik} \sim N(d_k, \sigma^2)$ $d_k \sim N(0, 10000)$ $\mu_i \sim N(0, 10000)$ $\sigma \sim Unif(0.01,2)$	**Data** $r_{ik} \sim Bin(n_{ik}, p_{ik})$ **Model** $logit(p_{ik}) = \mu_i + \delta_{ik}$ where δ_{ik} is the random effect of the k^{th} drug versus the placebo in the i^{th} study **Prior** $\delta_{ik} \sim N(d_k, \sigma_k^2)$ $d_k \sim N(0, 10000)$ $\mu_i \sim N(0, 10000)$ $log\sigma_k = log\sigma_0 + v_k$ $\sigma_0 \sim Unif(0.01,2)$ $v_k \sim N(0, \psi^2)$	**Data** $r_{ik} \sim Bin(n_{ik}, p_{ik})$ **Model** $logit(p_{ik}) = \mu_i + \delta_{ik}$ where δ_{ik} is the random effect of of the k^{th} drug versus the placebo in the i^{th} study $d_{23} = d_{13} - d_{12} + w_{123}$ w_{123} is the amount of inconsistency between direct and indirect comparison **Prior** $\delta_{ik} \sim N(d_k, \sigma^2)$ $d_k \sim N(0, 10000)$ $\mu_i \sim N(0, 10000)$ $w \sim N(0, \sigma_w^2)$ $\sigma, \sigma_w \sim Unif(0.01,2)$
[Example] Study 1: A vs. B vs. C trial (A is placebo)			
Data $r_{1A} \sim Bin(n_{1A}, p_{1A})$ $r_{1B} \sim Bin(n_{1B}, p_{1B})$ $r_{1C} \sim Bin(n_{1C}, p_{1C})$ **Model** $logit(p_{1A}) = \mu_1$ $logit(p_{1B}) = \mu_1 + d_B$ $logit(p_{1C}) = \mu_1 + d_C$ **Prior** $d_B, d_C \sim N(0, 10000)$ $\mu_1 \sim N(0, 10000)$	**Model** $logit(p_{1A}) = \mu_1$ $logit(p_{1B}) = \mu_1 + \delta_{1B}$ $logit(p_{1C}) = \mu_1 + \delta_{1C}$ **Prior (assume ρ=0.5)** $\begin{pmatrix}\delta_{1B}\\ \delta_{1C}\end{pmatrix} \sim MVN(\begin{pmatrix}d_B\\ d_C\end{pmatrix}, \sigma^2 \begin{pmatrix}1 & 0.5\\ 0.5 & 1\end{pmatrix})$ ➔ $\delta_{1B} \sim N(d_B, \sigma^2)$ ➔ $\delta_{1C} \mid \delta_{1B} \sim N(d_C + \frac{1}{2}(\delta_{1B} -$ $d_B, d_C \sim N(0, 10000)$ $\mu_1 \sim N(0, 10000)$ $\sigma \sim Unif(0.01,2)$	**Model** $logit(p_{1A}) = \mu_1$ $logit(p_{1B}) = \mu_1 + \delta_{1B}$ $logit(p_{1C}) = \mu_1 + \delta_{1C}$ **Prior (assume ρ=0.5)** $\begin{pmatrix}\delta_{1B}\\ \delta_{1C}\end{pmatrix} \sim MVN(\begin{pmatrix}d_B\\ d_C\end{pmatrix}, \begin{pmatrix}\sigma_1^2 & 0.5\sigma_{12}\\ 0.5\sigma_{12} & \sigma_2^2\end{pmatrix})$ ➔ $\delta_{1B} \sim N(d_B, \sigma_1^2)$ ➔ $\delta_{1C} \mid \delta_{1B} \sim N(d_C + \frac{1}{2}(\delta_{1B} -$ $d_B, d_C \sim N(0, 10000)$ $\mu_1 \sim N(0, 10000)$ $log\sigma_B = log\sigma_0 + v_B$ $log\sigma_C = log\sigma_0 + v_C$ $\sigma_0 \sim Unif(0.01,2)$ $v_B, v_C \sim Unif(0.01,2)$	Study 1: A vs. B vs. C trial Study 2: A vs. B Study 3: A vs. C ➔ We can estimate w_{ABC} because we can get the equation such that $d_{BC} = d_{AC} - d_{AB} + w_{ABC}$ Model and priors are similarly defined as in Model2. Additional prior is $w_{ABC} \sim N(0, \sigma_w^2)$

Appendix B

#BUGS code for Model 2 under the Bayes1 prior with respect to the UI improvement outcome

```
model {
for (i in 1:NS) {
s[i,1] <- 0
delta[i, t[i,1]] <- 0
mu[i] ~ dnorm(0, 0.0001)

for (k in 1:na[i]) {
      r[i,k] ~ dbin(p[i,t[i,k]], n[i,k])
      logit(p[i,t[i,k]]) <- mu[i] + delta[i,t[i,k]]
    }

for (k in 2:na[i]) {
      delta[i,t[i,k]] ~ dnorm(md[i,t[i,k]], taud[i,t[i,k]])
      md[i,t[i,k]] <- d[t[i,k]] - d[t[i,1]] + ss[i,k]
taud[i,t[i,k]] <- tau*2*(k-1)/k
      s[i,k] <- (delta[i, t[i,k]] - d[t[i,k]] + d[t[i,1]])
ss[i,k] <- sum(s[i, 1:k-1])/(k-1)
    }
  }

d[1] <- 0
for (k in 2:NT) {
d[k] ~ dnorm(0,0.0001)
ed[k] <- exp(d[k])         # ed is odds ratio against placebo
  }

sd~dunif(0.01,2)
tau<- 1/pow(sd,2)
var<- pow(sd,2)

  # pairwise ORs
  # Example: or[2,3] = odds ratio of active(2) vs. control(3)
for (k in 1:NT) {
for (c in 1:NT) {
lor[k,c] <- d[k] - d[c]
log(or[k,c]) <- lor[k,c]
    }
  }

  # difference of posterior probabilities
for (k in 2:NT) {
    PP[k] <- exp(mP+d[k])/(1+exp(mP+d[k])) - exp(mP)/(1+exp(mP))
  }

  # posterior probabilities
for (k in 1:NT) {
    pp[k] <- exp(mP+d[k])/(1+exp(mP+d[k]))
  }

  # ranking
mP<- mean(mu[1:27])         # Take average of mu[]
```

#BUGS code for Model 2 under the Bayes1 prior with respect to the UI improvement outcome (continued)

```
for (k in 1:NT) { logit(T[k]) <- mP + d[k] }     # T=prob of each trt
for (k in 1:NT) {
rk[k] <- NT + 1 - rank(T[],k)
best1[k] <- equals(rk[k],1)
best2[k] <- equals(rk[k],2)
best12[k] <- best1[k] + best2[k]
  }
}


#Init
list(
d=c(NA,0,0,0,0,0,0,0),
sd=1,
mu=c(0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0,  0,0,0,0,0, 0,0,0,0,0,  0,0,0)
)

#Data
list(NT=8, NS=28)
```

r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]
113	334	293	679	256	684	1	3	7	3
32	337	102	685	79	690	1	3	7	3
167	430	291	452	140	227	1	3	7	3
287	480	709	963	654	974	1	3	7	3
27	57	58	118	59	118	1	4	7	3
31	122	129	244	100	239	1	4	7	3
60	127	160	268	NA	1	1	2	NA	2
15	109	28	108	NA	1	1	2	NA	2
47	133	122	266	NA	1	1	2	NA	2
137	445	182	438	NA	1	1	3	NA	2
15	52	26	63	NA	1	1	4	NA	2
1	25	10	28	NA	1	1	4	NA	2
16	29	22	28	NA	1	1	4	NA	2
20	65	37	67	NA	1	1	4	NA	2
43	72	116	145	NA	1	1	4	NA	2
1	38	4	46	NA	1	1	4	NA	2
0	21	2	23	NA	1	1	4	NA	2
11	49	19	49	NA	1	1	5	NA	2
94	202	264	391	NA	1	1	5	NA	2
12	88	55	176	NA	1	1	5	NA	2
109	382	196	386	NA	1	1	6	NA	2
206	367	260	372	NA	1	1	6	NA	2
218	508	294	507	NA	1	1	7	NA	2
64	207	156	410	NA	1	1	7	NA	2
58	211	79	202	NA	1	1	7	NA	2
141	261	186	262	NA	1	1	8	NA	2
8	326	5	327	NA	1	1	8	NA	2
53	116	50	112	NA	1	4	7	NA	2

```
END
```

Appendix C

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
Abrams, 1998[1] Study: RCT Sample: 293	Men and women aged ≥18 years having urodynamically confirmed bladder overactivity, an increased frequency of micturition (≥8 micturitions/24h) and urge incontinence (≥1 incontinent episode/24h) and /or urgency during a 2-week washout/run-in period	Clinically significant stress incontinence; detrusor hyper-reflexia; hepatic, renal or hematological disorders; symptomatic or recurrent urinary tract infection; bladder outlet obstruction; those receiving bladder training, electro stimulation therapy; those with an indwelling catheter or who were on intermittent catheterization; pregnant or nursing women; or women of childbearing age who were not using reliable contraception	Tolterodine	Oxybutynin	Pharmacia and Upjohn AB, Uppsala. Sweden
Appell, 1997[2] Pooled Country: not reported N: 1120	Pooled analysis of 4 RCTS: men and women with detrusor overactivity (phasic detrusor contraction with an amplitude 2 10 cm H,O); and 4) urinary frequency (an average of 28 micturitions/24 hours) and urge incontinence (an average of ≥1 incontinence episode/24 hours) or urinary frequency.	Clinically significant stress incontinence; hepatic or renal disease; recurrent urinary tract infections (UTIs); interstitial cystitis; uninvestigated hematuria or hematuria secondary to malignant disease; indwelling catheter or intermittent catheterization; treatment with any investigational drug in the 2 months prior to entry; previous treatment with Tolterodine; electro stimulation therapy or bladder training within 14 days prior to entry or initiation during the study; treatment with any anti-cholinergic drug or any drug for urinary incontinence	Tolterodine 2 mg twice daily; tolterodine 1 mg twice daily; oxybutynin (5 mg three times daily)	Placebo	Not reported

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		within 14 days prior to the baseline visit or initiation during the study; unstable dosage of any treatment with anticholinergic side effects of initiation of such treatment during the study; previously demonstrated serious side effects on oxybutynin; an average total voided volume >3,000ml/24 hours; and clinically significant voiding difficulty with risk of urinary retention.			
Appell, 2001[3, 4] The OBJECT (Overactive Bladder: Judging Effective Control and Treatment) US N: 378	Participants with overactive bladder who had between 7 and 50 episodes of urge incontinence per week and 10 or more voids per 24 hours were included. Those with mixed stress and urge incontinence were eligible if the majority of the leakage accidents were related to urge incontinence.	Urinary tract infection, prostatitis, interstitial cystitis, urinary tract obstruction, urethral diverticulum, bladder tumor, bladder stone, prostate cancer were excluded, as were those who had delivered a baby or undergone pelvic, vaginal, bladder, or prostate surgery less than 6 months before study enrollment; participants with a post-void residual urine volume of more than 150ml at the time of screening; those at considerable risk of developing complete urinary retention if placed on an anti-muscarinic agent; those with clinically important medical problems or other organ abnormalities or pathologies for whom administration of extended-release oxybutynin or Tolterodine would present undue risk (medically uncontrolled cardiovascular, pulmonary, gastrointestinal,	10 mg/d of extended-release oxybutynin chloride	2 mg twice daily of tolterodine tartrate	AlZA Corporation, Mountain View, California

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		renal, endocrine, neurological, autoimmune, hematological, urological, or psychiatric disorders; severely reduced hepatic function or renal impairment); subjects with hematuria, or a positive urine culture; those with narrow-angle glaucoma; obstructive uropathy; myasthenia gravis; pelvic organ prolapse to the hymenal ring; gastrointestinal conditions such as partial or complete obstruction, preexisting severe gastrointestinal narrowing (pathologic or iatrogenic), decreased gastrointestinal motility (paralytic ileus, intestinal atony, chronic and severe constipation), or risk of gastric retention; those who had taken an investigational drug within the previous month; those with known allergies or hypersensitivities to oxybutynin chloride, tolterodine tartrate, or components of the respective drugs; current alcohol or other drug abuse; women who were pregnant or breastfeeding; those who were not capable of following the study schedule or directions; and those who were not able to swallow the medication without chewing, crushing, biting, dividing, or dissolving the capsule			
Burgio, 1998[5-7] RCT USA	Adults with at least 2 urge accidents per week on the 2-week	Continual leakage, post void residual urine volume >200 mL, uterine prolapse past the	Oxybutynin chloride, possible range of doses, 2.5 mg daily to	Behavioral Training: biofeedback-assisted PFMT/ placebo	Grants AG08010

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
N: 197	baseline bladder diary, and urge incontinence had to be the predominant pattern (the number of urge accidents had to exceed the number of stress accidents). Also, there had to be urodynamic evidence of bladder dysfunction (detrusor instability filling or provocation or maximal cystometric capacity of ≤350ml).	introitus, narrow-angle glaucoma, unstable angina, decompensated congestive heart failure, history of malignant arrhythmias, or impaired mental status (MMSE score <20).	5.0 mg 3 times daily		
Cardozo, 2006[8] Pooled NR N: 3,298	Men and women at least 18 years of age with a mean of >8 micturitions/day; >1 incontinence episode/day; >1 urgency episode/day	Reported previously	Solifenacin 5 mg; solifenacin 10mg	Placebo	Grant from Yamanouchi Pharmaceutical Co., Ltd., Tokyo, Japan.
Chapple, 2007[9, 10] RCT Belgium, Bulgaria, Czech Republic, Estonia, France, Germany, Hungary, Italy, the Netherlands, Poland, Romania, Russia, Spain, Sweden, Ukraine, the United Kingdom, South Africa, Australia, and New Zealand N: 1,135	Men and women with OAB symptoms with urinary urgency for >6 months and >3 UUI episodes per 24 hours (symptoms were recorded in a 3-day diary).	Pregnancy ;non adequate contraception throughout the trial; lower urinary tract pathology that could, in the investigator's opinion, be responsible for urgency or incontinence (e.g., genuine stress incontinence, bladder stones, interstitial cystitis urothelial tumours), pelvic prolapse of grade III or higher, clinically relevant bladder outlet obstruction, polyuria (>3 l per 24 hours), symptomatic or recurrent urinary tract infections, or post void residual (PVR) urine volume >100 ml; currently receiving treatment,	Tolterodine ER 4 mg, fesoterodine 4 mg, fesoterodine 8 mg	Placebo	Schwarz BioSciences GmbH and Pfizer Inc

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		were treated within 2 weeks of screening visit with antimuscarinic agents, were treated within the past 4 weeks with electro stimulation for bladder training, or had an active urinary tract infection or an underlying neurological disease responsible for their OAB; cardiac arrhythmia and/or unstable angina or a QTcB interval >500 ms.			
Chapple, 2007[11] RCT USA, Poland, South Africa, Hungary, Sweden, UK and Germany N: 400	Men and women >65 years of age with OAB for at least 6 month with >1 urge UI/day and >10 micturitions/day	Dependent toileting, dependent diary completion, taking drugs that can affect bladder function or external urethral sphincter, total daily volume >3000ml, mean volume/micturition >300ml, clinically significant stress UI or bladder outlet obstruction (post void residual volume >100ml); marked cystocele, stage 3 or 4 pelvic prolapse; participation in bladder training program or electrical stimulation therapy within 3 months of screening; intermittent urinary tract infection, clinically significant congenital or acquired disorder of the urinary tract, chronic pain syndrome or other clinically significant medical conditions including cognitive impairment, uncontrolled severe hypertension, uncontrolled severe heart failure, recent myocardial infarction, or uncontrolled thyroid disease.	Darifenacin (7.5 mg once daily for 2 weeks, then optional titration to 15 mg daily)	Placebo	Not reported

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
Chapple, 2005[12] RCT USA N: 65	Men and women aged 18–75 years with cystometric evidence of detrusor overactivity within the previous 6 months, either idiopathic or neurogenic (secondary to a neurological lesion present for >12 months), with >2 associated symptoms (average of >7 micturitions/day, >7 episodes of urgency/week, >1 urge incontinence episode/week necessitating change of clothing or pads).	Previous bladder surgery for detrusor overactivity; prostatectomy in the last 6 months; bladder stones; treatment with diuretics, antimuscarinic, tricyclic antidepressants or digoxin within the previous 2 weeks; stress and mixed incontinence, unless detrusor overactivity was the principal urodynamic observation and the patient was experiencing normal recommended limits, contraindications to anticholinergics (e.g. untreated or narrow angle glaucoma, bladder outlet obstruction).	Darifenacin immediate release (IR) 2.5 mg three times a day (t.i.d.); darifenacin controlled release (CR) 15 mg once daily (q.d.); darifenacin CR 30 mg q.d.	Oxybutynin 2.5 mg t.i.d.; oxybutynin 5 mg t.i.d.; oxybutynin 5 mg t.i.d.	Pfizer Inc
Chapple, 2005[13] Pooled Country: not reported N: 1,059	Men and women aged ≥18 years with symptoms of OAB for ≥6 months, and capable of independent toileting, with 5–50 episodes of incontinence per week during the run-in period, and a high voiding frequency (a mean of ≥8 voids/24 hours) and urgency (a mean of ≥1 episode/24 hours); women of childbearing potential required to use an adequate method of contraception throughout the study;	Initiation of a bladder training; pregnancy and lactation; clinically significant stress incontinence (i.e.>1 episode of stress incontinence per week), BOO and/or a post void residual urine volume of > 200 mL (as measured by pelvic ultrasonography); clinically important medical problems that would interfere with the patient's participation in the study; patients with interstitial cystitis, severe constipation (two or fewer bowel movements per week), hematuria or intermittent UTI; cystocele or other clinically significant pelvic prolapsed; patients with an indwelling	Darifenacin 7.5 mg or 15 mg/day	Placebo	The studies were funded by Pfizer Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	those taking hormone–replacement therapy had to have received such therapy for ≥2 months before entering the study; men taking finasteride for BPH had to be on a stable dose for ≥2 months; those receiving long-term therapy with diuretics, antihypertensive medications, benzodiazepines or antihistamines had to be taking a stable dose before study recruitment, with no plans to change treatment during the study; and patients on bladder training program were not to modify or discontinue their training during the course of the study.	catheter and those who practiced intermittent self-catheterization; urogenital surgery in the previous 6 months; patients with contraindications to antimuscarinic therapy (e.g., uncontrolled narrow-angle glaucoma, urinary retention, gastric retention); history of alcohol/drug abuse; and known hypersensitivity to study medication.			
Chapple, 2004[14] Study: RCT Sample: 728	Not reported	Not reported	Fesoterodine	Placebo	Not reported
Chapple, 2004[15] Study: RCT Sample: 1081	Men and women aged>=18 years with symptomatic OAB (including urgency, urge incontinence, or frequency) for >=3 months. After run-in period patients had to have had an average frequency of >=8	Significant BOO, a post void residual volume of >200mL, incontinence for which stress was determined to be the predominant factor, presence of a neurological cause for detrusor muscle overactivity, evidence of UTI or bladder stones, previous pelvic irradiation, or previous or	Solifenacin 5mg and 10mg	Tolterodine 2mg twice daily or placebo	Yamanouchi Pharma Co., Ltd, Tokyo,Japan

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	voids/24 hours and have experienced at least 3 episodes of urgency and/or three episodes of incontinence during the 3-day voiding diary period.	current malignant disease of the pelvic organs, any medical condition contraindicating the use of antimuscarinic medication (including narrow-angle glaucoma and urinary or gastric retention), nonpharmacological treatment for OAB including electro stimulation therapy or start of a bladder training program during the 2 weeks before or during the study, diabetic neuropathy, use of drugs intended to treat incontinence, use of any drugs with cholinergic or anticholinergic side-effects, and participation in a clinical trial within 30 days before the study entry; pregnant or nursing women, women of child-bearing potential intending to become pregnant during the study or who were not going to use reliable contraceptive methods.			
Chapple, 2004[16] Study:RCT Sample:1049	Patients with urge incontinence, frequency of micturition, and urinary urgency.	Not reported	Darifenacin	Placebo	Not reported
Choo, 2008[17] Study: H5 Sample: 357	Men and women aged ≥18 years with symptoms of OAB for ≥3months; average frequency of ≥8 voids per 24h and experienced at least three episodes of	Clinically significant bladder outlet obstruction, a PVR volume of >200ml, incontinence for which stress was determined to be the predominant factor, presence of a neurological cause for detrusor muscle overactivity,	Solifenacin 5mg/10mg	Tolterodine 4mg	Research grant from Astellas Pharma Inc., Tokyo, Japan

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	urgency or three episodes of urgency incontinence during the 3-day voiding diary period	evidence of urinary tract infection or bladder stones, previous pelvic irradiation, or previous or current malignant disease in the pelvic organs, any medical condition contraindicating the use of antimuscarinic medication(including narrow angle glaucoma and urinary or gastric retention), non-pharmacological treatment for OAB including electro stimulation therapy or start of a bladder training program during the 2 weeks before or during the study, diabetic neuropathy, use of drugs intended to treat incontinence, use of any drugs with cholinergic or anitcholinergic side effects and participation in a clinical trial within 30 days before study entry; women of child-bearing potential who were pregnant or nursing, intending to become pregnant during the study, or who were not using reliable contraceptive methods.			
Chu, 2009[18] Study: RCT Sample: 672	Men and women aged ≥18 years with a diagnosis of OAB made by an investigator based on symptoms (urinary frequency, urgency, or urge incontinence); had to record a mean of >=8 micturitions per 24 hours plus a mean	Stress urinary incontinence or mixed urinary incontinence in which stress was predominant (mixed incontinence was otherwise allowed), a neurologic cause of detrusor overactivity, urinary retention, grade III/IV prolapse with cystocele, and recurrent or active urinary tract infection; patients with	Solifenacin	Placebo	Funded and sponsored by Astellas Pharma Inc., Tokyo, Japan

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	of ≥1 incontinence episode per 24hours and/or a mean of ≥1 urgency episode per 24 hours	abnormal findings on 12-lead ECG or abnormal laboratory findings. Women of childbearing potential were required to have a negative serum pregnancy test at screening and to use a medically acceptable form of contraception during study participation			
Diokno, 2003[19-22] OPERA (Overactive bladder: Performance of Extended Release Agents) trial USA N: 790	OPERA (Overactive bladder: Performance of Extended Release Agents):Women with OAB, aged 18 years and older, who documented 21 to 60 UUI episodes per week and an average of 10 or more voids per 24 hours; predominant urge UI; with or without history of prior treatment with an anticholinergic drug for OAB.	Treatable genitourinary conditions that could cause incontinence, 2 post void residual urine volumes shown by ultrasonography to exceed 150 mL; pronounced risk of developing complete urinary retention, clinically important medical problems that would put a participant at undue risk of anticholinergic effects, hematuria, uncontrolled narrow-angle glaucoma, obstructive uropathy, reduced gastrointestinal motility, and known hypersensitivity to the study medications.	Extended-release formulations of oxybutynin at 10 mg/d	Tolterodine at 4 mg/d	ALZA Corporation, Mountain View, California, and Ortho-McNeil Pharmaceutical, Raritan, NJ
Dmochowski, 2010[23] Study:RCT Sample:896	Men and women aged >=18 years with OAB symptoms for >=3 months before screening, recorded a mean of >=8 micturitions per 24 hours and >= 3 urgency episodes per 24 hours in a 3-day bladder diary at baseline, and rated their bladder condition at baseline as causing	Patients with a history of acute urinary retention requiring catheterization, severe voiding difficulties in the judgment of the investigator, urinary incontinence symptoms attributed by the investigator primarily to stress urinary incontinence, significant pelvic organ prolapse or lower urinary tract surgery within the preceding 6 months, clinically significant	Fesoterodine	Placebo	Funded by Pfizer, Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	at least some moderate problems using the Patient Perception of Bladder Condition (PPBC).	hepatic or renal diseases, neurologic disease that significantly affected bladder function, treatment with an antimuscarinic OAB medication or potent CYP3A4 inhibitor within 2 weeks of screening, and any contraindication to fesoterodine. Also excluded were men with intermittent or unstable use of alpha blockers or 5-alpha reductase inhibitors (consistent use was permitted) or who started such treatment within 4 weeks of screening.			
Dmochowski, 2008[24] RCT USA N: 564	Men and women aged 18 years or older with OAB of 6 months' or longer duration with symptoms of urinary frequency (a mean of 10 or more toilet voids per day), urgency (1 or more episodes of severe urgency associated with a toilet void), and UUI (a mean of 1 or more UUI episodes per day).	Total voided volumes greater than 3000 mL/day or a mean volume voided/void greater than 250 mL; predominantly stress, insensate, or overflow incontinence; history of neurogenic bladder, indwelling or intermittent catheterization, significant renal disease (defined as serum creatinine greater than 1.5 mg/dL), uninvestigated hematuria or urinary tract infection during screening, or a history of more than 3 urinary tract infections in the previous 12 months; other bladder pathologies, including clinically significant retention (defined as post void residual urine volume greater than 100 mL), cancer, and interstitial cystitis; prostate specific	Trospium chloride 60 mg once daily	Placebo	Esprit Pharma and Indevus Pharmaceuticals Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		antigen level greater than 4 ng/mL, prostate cancer, or chronic prostatitis.			
Dorschner, 2000[25] RCT Country: Not reported N: 107	Men and women older than 60 years of age with urgency, urge incontinence, or mixed urge-stress incontinence, >1 episode of UI/day and micturition volume <300ml/micturition	Acute urinary tract infections, mechanical or functional bladder-emptying disorders, residual urine >20% of voided volume by ultrasound, micturition volume >300ml in uroflow, renal insufficiency, concomitant medications interfering with the drug studied (neurotropic/ musculotropic spasmolytics, centrally acting muscle relaxants, psychopharmacological agents or drugs for the treatment of Parkinson's disease, anti-arrhythmic), serious life threatening cardiovascular diseases (myocardial infarction within the previous 3 months, unstable coronary heart disease, implanted cardiac pace-maker, decompensated myocardial insufficiency, tachycardia or bradycardia at rest, second-or third-degree atrio-ventricular block, complete bundle branch interventricular heart block, chronic atrial fibrillation and ventricular extrasystoles Lown IVb in the pre-study ECG monitoring.	Propiverine (15 mg t.i.d.)	Placebo	Grant provided by Apogepha

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
Drutz, 1999[26] RCT United States and Canada N: 277	Age ≥18 years; all female patients were to be postmenopausal, surgically sterile, or using an adequate contraceptive method before and during the study; evidence of detrusor overactivity on subtracted cystometry (phasic detrusor contraction with an amplitude ≥10cmH_2O), along with urinary frequency (≥8 micturitions on average per 24 hours) and either urge incontinence (≥1 incontinence episode on average per 24 hours), as confirmed by micturition diaries during the run-in period, and/or urinary urgency.	Clinically significant stress incontinence as determined by the investigator during a cough stress test maneuver; hepatic or renal disease; any disease which the investigator thought made the patient unsuitable for inclusion; recurrent urinary tract infections; interstitial cystitis; uninvestigated hematuria or hematuria secondary to malignant disease; indwelling catheter or intermittent catheterization; treatment with any investigational drug in the 2 months prior to entry; previous treatment with tolterodine; electro-stimulation therapy or bladder training within 14 days prior to entry or initiation during the study; treatment with any anticholinergic drug, or any drug for urinary urge incontinence within 14 days prior to the baseline visit or initiation during the study; unstable dosage of any treatment with anticholinergic adverse effects or initiation of such treatment during the study; previously demonstrated serious adverse effects on oxybutynin average total voided volume/24 hours of >3000 ml; or clinically significant voiding difficulty with risk of urinary retention (such as residual volume >200 ml or urine flow rate <10ml/s).	Tolterodine 2mg b.i.d. or oxybutynin 5mg t.i.d.	Placebo	The study was funded by Pharmacia & Upjohn AB, Uppsala, Sweden

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
Goode, 2004[7] RCT analysis USA N: 197	Subjects were community-dwelling women aged ≥55 years who were recruited to a university based continence clinic through professional referrals and advertising. They had urge incontinence or mixed incontinence with urge as the predominant pattern. All patients were ambulatory and not demented. They had urodynamic evidence of bladder dysfunction, either detrusor overactivity (DO) or a maximal cystometric capacity ≥350 mL.	Not reported	Behavioral therapy	Oxybutynin 2.5mg/day to 5mg t.i.d. or Placebo	NIH Grant
Halaska, 2003[27] RCT Austria, Bulgaria, Czechoslovakia, Germany, Russia and Spain N: 358	Men and women >18 years of age with urge syndrome (undue frequency of micturition, nocturia, overwhelming urge, wetting), urge incontinence, urge incontinence as one component of mixed incontinence, or urge incontinence due to a neurological condition (detrusor hyperreflexia) as confirmed using urodynamic measurements.	Absolute tachycardia; closed-angle glaucoma; myasthenia gravis; severe arteriosclerosis of the cerebral vessels; stress incontinence; undue frequency of micturition due to heart failure, renal failure or diuretic therapy; Bladder outlet obstruction; Acute urinary tract infection at the beginning of the trial; Hiatus hernia in combination with reflux esophagitis; stenoses in the gastrointestinal tract; megacolon; colonic ulceration; allergy or intolerance towards atropine,	Trospium chloride (20 mg twice daily) or	Oxybutynin (5 mg twice daily).	Not reported

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		OXY, TCI or other constituents of the trial medication; concurrent medication with anticholinergics, tricyclic or tetracyclic antidepressants, a-blockers or b-sympathomimetics within the last 7 days before starting the trial; urological or gynecological operations within the last 3 months before starting the trial; serious illnesses or conditions which would preclude participation in any clinical trial (malignant neoplasms, alcoholism, drug misuse); pregnancy or lactation; participation in any other study.			
Herschorn, 2010[28] Study:RCT Sample:1712	Men and women aged ≥18 years, with symptoms of OAB (self-assessed) for ≥3 months before screening and a mean of one or more UUI episode/24 h and ≥ 8 voids/24 h reported in 3-day bladder diaries completed at baseline.	Patients with clinically significant hepatic or renal disease; lower genitourinary pathology or surgical treatment thereof responsible for voiding dysfunction; neurological conditions such as stroke, multiple sclerosis, spinal cord injury, or Parkinson's disease; previous history of acute urinary retention requiring catheterization; symptoms of incontinence being predominately stress UI in the opinion of the investigator; treatment with antimuscarinic OAB medication within 2 weeks before screening; or use of any electrostimulation,	Fesoterodine	Placebo	Sponsored by Pfizer Inc.Editorial assistance was provided by Simon J. Slater, PhD and Colin P.Mitchell, PhD from Complete Healthcare Communications, Inc. and was funded by Pfizer Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		bladder training, or pelvic floor exercises within 4 weeks of screening. Female patients of childbearing potential who were heterosexually active without using an adequate form of contraception, or who were pregnant, nursing, or with a positive urine pregnancy test were also excluded.			
Herschorn, 2008[29] Study: RCT Sample: 617	≥18 years of age; mean of ≥8 micturitions per 24 hours and ≥3 episodes of urgency or urgency urinary incontinence (UUI) in a 3-day bladder diary before randomization; experienced OAB symptoms for ≥3 months and at least moderate problems associated with their most bothersome OAB symptom, as reported on the OAB Bother Rating Scale	If received any drug used to treat UUI or OAB within 14 days before the study treatment period	Tolterodine-ER	Placebo	Funded by Pfizer Inc
Hill, 2006[30] Darifenacin Study Group. Country: Not reported N: 439	Male and female patients, aged >18 years, with urge incontinence (>10 episodes over 14 days), high micturition frequency (mean of >8 eight voids per day), and urinary urgency (a strong desire to void on average at least once per day) for at least 6	Clinically significant stress incontinence, bladder outlet obstruction or a postvoid residual urinary volume >200 ml; local pathology that could cause urinary symptoms (e.g., interstitial cystitis, bladder stones, severe constipation (≤2 bowel movements per week), history of intermittent urinary tract infections; those who had undergone urogenital	Darifenacin (Novartis Pharma AG, Basel, Switzerland) once-daily 7.5, 15, 30 mg	Placebo	The study was funded by Pfizer Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	months, regardless of previous antimuscarinic treatment.	surgery within the previous 6 months, or cystoscopy in the previous 30 days; patients with indwelling catheter or using intermittent self-catheterization; presence of clinically significant systemic disease; patients who intended to start a bladder-training program during the study, or had contraindications to antimuscarinic therapy; pregnant and lactating women; no concomitant treatment with drugs (including drugs with significant anticholinergic effects), opioids, hormone replacement therapy (unless taken for >2 months), and drugs known to be significant inhibitors of cytochrome P450 2D6 or 3A4 isoenzymes (cimetidine, fluoxetine, ketoconazole, itraconazole, etc.).			
Homma, 2003[31-33] Japanese and Korean Tolterodine Study Group Korea and Japan N: 608	Men and women aged >20 years with symptoms of urinary urgency, urinary frequency (> 8 voids/24 hours), urge incontinence (>5 episodes/ week) and symptoms of OAB for >6 months were eligible for inclusion. Patients were recruited based solely on their symptoms of OAB, irrespective of	Demonstrable stress incontinence; total daily urine volume of >3 L; average volume voided/ void of >200 mL; significant hepatic or renal disease; any contraindication to anticholinergic treatment, e.g. uncontrolled narrow-angled glaucoma, urinary retention or gastric retention; symptomatic or recurrent UTI; interstitial cystitis; haematuria or BOO; an indwelling catheter or	Tolterodine 4mg capsules once daily	Oxybutynin 3mg tablets three times daily, placebo	This study was supported by a grant from Pharmacia Corporation.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	whether they had received previous antimuscarinic treatment and irrespective of their response to such therapy.	intermittent self-catheterization; and electro-stimulation or bladder training within 14 days before randomization or expected to commence during the study period; pregnant or nursing women and women of childbearing potential not using reliable contraception.			
Jacquetin, 2001[34] RCT Belgium and France N: 251	Male and female patients aged ≥18 years were eligible for inclusion in the study if they had urodynamically proven overactive bladder, and symptoms of urgency and/or urge incontinence (≥1 incontinence episode/24 hours) with increased frequency of micturition (≥8 micturitions/24 hours) irrespective of prior treatment or treatment failure.	Significant stress incontinence; hepatic or renal disease; symptomatic or recurrent urinary tract infection (UTI); interstitial cystitis; haematuria; clinically significant voiding difficulty; patients receiving bladder training, electro-stimulation therapy or having an indwelling catheter or on intermittent catheterization; pregnant or nursing women, or women of childbearing age who were not using reliable contraception.	Tolterodine 1 or 2mg twice daily	Placebo	Pharmacia Corporation
Johnson, 2005[35] RCT analysis USA N: 131	To be included in the study, participants had to report at least two accidents per week and to demonstrate the ability to complete an interpretable bladder diary that confirmed this frequency of urine loss. Urge incontinence had to	Participants with continual leakage, elevated postvoid residual urine volume (4200 mL), narrow angle glaucoma, uterine prolapse past the vaginal introitus, unstable angina pectoris, decompensated congestive heart failure, or impaired mental status (MMSE score 20) were excluded.	Behavioral training, drug treatment (oxybutynin IR titrated from 2.5 mg per day to 5.0 mg three times a day)	Placebo	Supported by grant from the National Institute on Aging. Dr. Johnson received additional support from the Emory University Center for Health in Aging. The John A. Hartford Foundation Southeast Center of Excellence in Geriatric Medicine and the Birmingham/

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	be the predominant pattern (urge accidents exceeded the number of stress and other accidents), with urodynamic evidence of bladder dysfunction. Two-channel supine water cystometry was performed to demonstrate detrusor instability (defined as urodynamic observation of involuntary detrusor contractions during the filling phase) or sensory urgency (defined as bladder capacity of less than 350 mL) for inclusion in the study.				Alabama VA GRECC provided infrastructural support that enabled this inter-institutional collaboration.
Junemann, 2000[36] Study: RCT Sample: 234	Patients with urge - syndrome (motor urge, sensory urge and combined motor urge and stress incontinence). Patients medical history and a urodynamic measurement (minimum one unstable detrusor contraction of 10 cm H2O or first desire to void at a bladder filling of <150ml) verified the diagnosis of urge-syndrome	NR	Trospium hydrochloride	Tolterodine and placebo	NR

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
Kaplan, 2010[37, 38] Study: RCT Sample: 2417	Subjects with OAB symptoms for >=months and recorded micturitions and >=1 urgency urinary incontinence episode per 24h in 3-day baseline diaries	NR	Fesoterodine	Tolterodine/Placebo	Sponsored by Pfizer Inc.
Karram, 2009[39, 40] Study: VENUS Sample: 739	This study, that is, the VENUS study enrolled patients aged>=18 years with OAB (at least 1 urgency episode with or without incontinence and >=8 micturitions per 24 hours) for >=3 months	Presence of stress or stress-predominant mixed urinary incontinence, chronic inflammation or cystitis, and clinically significant bladder outlet obstruction	Solifenacin	Placebo	Research grant from Astellas Pharma US, Inc. and GlaxoSmithKline
Kelleher, 2002[41-48] RCT USA N: 1015	Male and female patients aged 18 years or older with urinary frequency (average of ≥8 micturitions/24 hours over a 7-day period), urge incontinence (≥5 episodes/week), and symptoms of OAB for at least 6 months.	Other types of bladder dysfunction, with diseases that may have affected urinary output.	Tolterodine extended-release (ER) 4 mg once/day, or tolterodine immediate-release (IR) 2 mg twice daily	Placebo	Pharmacia Corporation
Khullar, 2004[49, 50] RCT UK N: 854	Women 18 years or older with urge-predominant mixed incontinence, including urge incontinence (five or more episodes per week), urinary frequency (eight or more micturitions on average in 24 hours), and urgency in combination with	Pure stress urinary incontinence; predominant stress urinary incontinence; a total daily urine volume greater than 3 L; suspected or documented hepatic or renal dysfunction; symptomatic urinary tract infection; interstitial cystitis, uninvestigated hematuria, or clinically significant bladder obstruction; any contraindication to	Tolterodine tartrate extended-release (ER) 4 mg	Placebo	Pfizer Inc

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	stress incontinence irrespective of the use of previous antimuscarinic treatment.	antimuscarinic treatment; and any nonsurgical treatment for incontinence within 4 weeks of the first study visit; treatment within 2 weeks before randomization with any drug for incontinence (except estrogen therapy started more than 2 months before the first visit); agonist or potent inhibitors of cytochrome P450 3A4 isoenzymes; pregnancy, lactation, or inadequate contraception.			
Lee, 2010[51] Study: Propiverine study on overactive bladder including urgency data N: 264	Men and women ages ≥18 years who had self-reported symptoms of OAB for ≥3months; average urinary frequency of ≥10 voids/24h and urgency of two or more episodes/24h defined as 'moderate to severe' in the Indevus Urgency Severity Scale(IUSS) during the 3-day voiding diary period before randomization	Clinically significant stress urinary incontinence (more than one episode per week); genitourinary conditions that could cause OAB symptoms, such as UTI; and contraindications to the use of antimuscarinic drugs	Propiverine hydrochloride 60 mg/d	Placebo	Sponsored by Jeil Pharmaceutical Co. Ltd., Seoul, Korea
Lee, 2002[52] RCT South Korea N: 228	Male and female subjects aged ≥18 years with symptoms of overactive bladder for ≥6 months were eligible for enrolment in the study. Symptoms, as measured by micturition diaries, were defined as urinary urgency and	(i) significant stress incontinence; (ii) women of childbearing age who were not using reliable contraception; (iii) pregnant or nursing women; (iv) treatment with any drug with known anticholinergic side-effects in the in the 2 weeks prior to the study; (v) significant renal or hepatic disease; (vi) any	Tolterodine 2mg bid	Oxybutynin 5mg bid	Grant from Pharmacia

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	frequency (≥8 micturitions on average per 24 hours), with or without urge incontinence. Patients were enrolled exclusively on the basis of symptoms (i.e. urodynamics was not performed), irrespective of whether they had received prior antimuscarinic therapy.	contraindication to antimuscarinic therapy (e.g. narrow-angle glaucoma, urinary or gastric retention, known hypersensitivity to tolterodine or oxybutynin); (vii) symptomatic acute or recurrent urinary tract infection; (viii) interstitial cystitis or hematuria; (ix) bladder outlet obstruction; and (x) patients receiving bladder training, electro-stimulation therapy or having an indwelling catheter or on intermittent catheterization.			
Lehtoranta, 2002[53] RCT Finland N: 9	Female or male patients aged 18–75 years were recruited to the study. They had to have a history of urgency or urge incontinence and cystometrically proven detrusor hyperreflexia or instability according to the ICS criteria (International Continence Society).	Stress incontinence and pure nocturnal enuresis were excluded.	Oxybutynin 5mg/30ml three times daily	Placebo(30ml of sterile saline)	Not reported
Madersbacher, 1999[54] RCT USA N: 366	History of urgency or urge incontinence, a maximum cystometric bladder capacity of ≤300 ml, age ≥18years and body weight ≥45kg.	Detrusor hyperreflexia, postoperative (bladder) incontinence, intravesical obstruction, a postvoid residual urine (PVR) of >15% of the maximal cystometric bladder capacity, acute UTIs, angina pectoris, glaucoma, megacolon, clinically relevant cardiac, renal or hepatic dysfunctions, tachy/dysrhythmias, frequency or nocturia due to heart or	Propiverine 15mg three times a day	Oxybutynin 5mg twice a day, placebo three times a day	Not reported

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		renal insufficiency, or overt cerebral sclerosis.			
Malone-Lee, 2009[55] RCT UK N: 307	Male and female subjects aged ≥18 years with urinary frequency (defined as an average of ≥8 voids/24 hours, measured over a 7-day period) and urgency (with or without UUI), symptoms of OAB for ≥6 months before randomization, with no significant stress UI and adequate contraception.	Mean volume voided of >300 mL/void or a mean total volume of urine >3000 mL/24 hours; significant hepatic or renal disease, symptomatic UTI, diagnosed interstitial cystitis, un-investigated hematuria, or clinically significant BOO; anticholinergic drugs or other treatments for OAB in the 14 days before randomization; known hypersensitivity to tolterodine-ER or any of its excipients; oral cytochrome P450 3A4 inhibitors (e.g. macrolide antibiotics), and electro-stimulation or bladder retraining in the 3 months before randomization.	Tolterodine-ER (4 mg capsule od)	Placebo	Pharmacia (now Pfizer Ltd)
Malone-Lee, 2001[56] RCT United Kingdom, France, and the Republic of Ireland N: 177	Older men and women (age ≥65 years) with symptoms of urinary urgency, increased frequency of micturition (≥8 micturitions/24 hours), and/or urge incontinence (≥1 episode/24 hours).	Significant stress incontinence, urinary outflow obstruction, urinary retention (as determined by palpation after voiding), symptomatic urinary infection, interstitial cystitis, unexplained hematuria, use of urinary catheterization or electro-stimulation, hepatic and renal disease with biochemical markers twice the upper limit of the normal reference range, concomitant antimuscarinic medication, previous treatment with tolterodine, and exposure to any other investigational drug in the preceding 2 months.	Tolterodine 1 mg or 2 mg twice daily	Placebo	Pharmacia & Upjohn AB

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
Moore, 1990[57] Study: RCT Sample: 53	Patients with involuntary detrusor contractions >30cm H2O during the filling phase of cystometry	Those with neurological and other urological disorders; patients with coexistent genuine stress incontinence, low compliance bladder, bacterial or interstitial cystitis, age greater than 75 years or previous treatment with oxybutynin	Oxybutynin hydrochloride	Placebo	Tillots Laboratories provided oxybutynin and placebo tablets
NCT00444925[58] Study: RCT N: 1712	Adult overactive bladder (OAB) patients who present with OAB symptoms, including urinary frequency ≥ 8 per day and urgency urinary incontinence ≥1 per day	Patients with conditions that would contraindicate for fesoterodine use, e.g., hypersensitivity to the active substance (fesoterodine) or to peanut or soya, urinary retention, and gastric retention; patients with significant hepatic and renal disease or other significant unstable diseases; and OAB symptoms caused by neurological conditions, known pathologies of urinary tract, etc.	Fesoterodine	Tolterodine/Placebo	Sponsored by Pfizer Inc.
Rentzhog, 1998[59] Study: RCT Sample: 81	Men and women aged 18-75 years; presence of symptoms of urinary urgency, increased frequency of micturition (at least 8 micturitions per 24 hours) and/or urge incontinence (at least one episode of incontinence per 24 hours) during a 1-week pre-study run-in period. All eligible patients should have had urodynamically confirmed detrusor instability (defined as a phasic increase in	Stress incontinence or detrusor hyperreflexia; clinically significant cardiac, hepatic, renal or hematological disorders; patients with contraindications to antimuscarinic agents; and pregnant or lactating women and women of childbearing age who were not using reliable contraception.	tolterodine	Placebo	Pharmacia and Upjohn AB, Uppsala. Sweden

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	detrusor pressure in the presence of typical symptoms) and a maximum urinary flow rate (Q max)of >=15mL/s (patients with a lower Qmax were eligible for inclusion provided there was no evidence of clinically significant bladder outlet obstruction), either sterile urine or clinically insignificant bacteriuria, and normal routine laboratory tests				
Rogers, 2009[60-62] Study: RCT Sample: 413	Women ≥18 years with OAB symptoms for>=3 months; mean of >=8 micturitions per 24 hours, including ≥0.6 UUI episodes and ≥3 OAB micturitions (i.e. micturitions associated with at least a moderate degree of urgency), in a 5-day bladder diary at baseline; subjects also reported being in a stable, sexually active relationship (self-defined) for ≥6 months and having at least some moderate problems related to their bladder condition on the Patient Perception of Bladder Condition.	One subject in the tolterodine group with an extreme increase in the number of UUI episodes per 24 hours from baseline to week 12 was identified as an influential outlier and was excluded from all efficacy analyses	Tolterodine-ER	Placebo	Funded by Pfizer Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	Heterosexual.				
Rogers, 2008[61] RCT USA N: 413	Women (aged ≥18 years) with a mean of greater than or equal to eight micturitions, ≥0.6 UUI episodes, and greater than or equal to three OAB micturitions (i.e., micturitions associated with moderate or severe urgency or UUI) per 24 hours with at least "some moderate problems" on the Patient Perception of Bladder Condition Questionnaire ; with OAB symptoms for ≥3 months and to have been in a stable, sexually active relationship (self-defined) with a male partner for ≥6 months.	Stage ≥3 pelvic organ prolapse, history of lower urinary tract surgery, lifelong sexual dysfunction unrelated to lifelong UUI, or predominant stress UI.	Tolterodine ER (4 mg)	Placebo	Pfizer Inc
Rudy, 2006[63] RCT analysis USA N: 658	Men and women ≥18 years old with OAB symptoms for ≥6 months, a minimum urinary frequency of 70 toilet voids per 7 days (i.e. mean ≥10 voids/day), and symptoms of urgency ; with at least seven UUI episodes/week.	Predominately stress, insensate, or overflow; neurogenic bladder disorders, significant renal disease, uninvestigated haematuria, >2 UTIs during the previous year; significant BOO, concurrent anticholinergic drug use or other drug therapy for OAB within 21 days before randomization, bladder surgery within 6 months, cancer, interstitial cystitis, men with PSA levels of ≥10 ng/mL, diuretic use, estrogen	Trospium chloride 20 mg twice daily	Placebo	Indevus Pharmaceuticals

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		therapy, and non-pharmacological bladder therapy that were not part of a stable, long-term program.			
Sand, 2009[9, 64, 65] Pooled USA N: 1971	Men and women ≥18 years of age who reported OAB symptoms for ≥6 months and demonstrated urinary frequency (≥8 micturitions per 24 hours) and either urinary urgency (≥6 total episodes) or UUI (≥3 total episodes) in 3-day bladder diaries at least moderate bladder problems on a six-point Likert scale: "My bladder causes me no problems (0), very minor problems (1), minor problems (2), moderate problems (3), severe problems (4), or very severe problems (5)."	Lower urinary tract pathology that could (in the investigator's opinion) be responsible for urgency or incontinence, significant pelvic prolapse (grade III or higher), clinically relevant bladder outlet obstruction, polyuria (>3 L/24 hours), symptomatic or recurrent urinary tract infections, postvoid residual volume >100 mL, and recent treatment with an antimuscarinic agent.	Fesoterodine 4 or 8 mg, or tolterodine extended release (ER) 4 mg	Placebo	Schwarz Bio- Sciences GmbH and Pfizer Inc.
Sand, 2009[66] Dmochowski, 2010[67] Pooled Country not reported N: 989	Subgroup analysis of women aged ≥18 years with OAB of ≥6 months' duration with urinary urgency (≥1 severe urgency severity rating on the validated Indevus urgency severity scale); urinary frequency (average ≥10 voids/day, occurring at any time	Predominantly stress, insensate, or overflow incontinence (as determined by investigators), demonstrable renal or urinary disorders including neurogenic bladder disorders, significant renal disease, uninvestigated hematuria, current or a history of ≥3 episodes of urinary tract infection in the preceding year, bladder	Trospium ER (60-mg capsules)	Placebo	Allergan, Inc. and Endo Pharmaceuticals (formerly Indevus Pharmaceuticals Inc.).

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	of the 24-hour period); and pure urge or mixed urinary incontinence with predominant UUI, with an average of ≥1 UUI episode/day.	outlet obstruction, interstitial cystitis, or bladder cancer; subjects requiring long-term diuretic or estrogen therapy.			
Staskin, 2006[68] Pooled Country not reported N: 3298	Pooled analysis of 4 RCTs of men and women over 18 years with OAB (mean of ≥8 voids/24 hours, plus ≥1 incontinence episode or ≥1 urgency episode/24 hours)	Women with a history of stress-predominant UI, positive cough-provocation test; no baseline assessment or no episodes of the individual diary symptom during the baseline diary screening period.	Solifenacin 5mg; Solifenacin 10mg;	Placebo	Yamanouchi Pharma Inc.
Staskin, 2007[69] Trospium Study Group. USA N: 601	Not reported	Not reported	Trospium chloride 60 mg/day	Placebo	Esprit Pharma and Indevus Pharmaceuticals
Staskin, 2004[70] RCT USA N: 658	Not reported	Not reported	Trospium chloride 20-mg twice daily	Placebo	Not reported
Staskin, 2009[71] RCT US N: 789	Men and women with OAB who were 18 years or older; urge or mixed UI with a predominance of urge UI episodes as well as a mean of 8 or more urinary voids per day and 4 or more urge UI episodes per day on a baseline 3-day bladder diary regardless of whether symptoms were of neurological origin. The bladder diary was to be independently completed by the patient. Patients	Potential participants were excluded from study based on criteria designed to rule out incontinence related to chronic illness, anatomical abnormality and concomitant medication.	OTG (oxybutynin chloride)	Placebo	Laboratory assessments were performed at Mayo Laboratory for Clinical Trials, Rochester, Minnesota

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	needed to have a mean voided volume of 350 ml or less during a 2-day urine collection period and a PVR of 250 ml or less on ultra-sonography or catheterization.				
Steers, 2005[72] RCT Canada, USA N: 395	Patients aged >18 years with symptoms of OAB for at least 6 months, capable of independent toileting. Irrespective of response to previous treatments patients had to have urge incontinence (>5 episodes per week), voiding frequency (>8 voids per day), and urgency (a strong desire to void at least once per day). Adequate method of contraception throughout the study for young women.	Contraindications to anticholinergic therapy (e.g., uncontrolled narrow-angle glaucoma, urinary retention or gastric retention); clinically significant stress incontinence, BOO and/or a postvoid residual urinary volume (PVR) of >200 mL ; pregnancy and lactation; genitourinary conditions that could cause urinary symptoms; fecal impaction or severe constipation (two or fewer bowel movements per week); urogenital surgery within the previous 6 months; bladder biopsy in the previous 30 days; indwelling catheter and intermittent self-catheterization; clinically significant disease; bladder-training program during the study; concomitant treatment with anticholinergic or antispasmodic drugs (including drugs with significant anticholinergic effects, e.g., imipramine), opioids and other drugs known to cause significant constipation, hormone replacement therapy (unless	Darifenacin controlled-release tablets 7.5 mg	Placebo	This study was funded by Pfizer Inc.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		taken for >2 months), and drugs known to be potent cytochrome P450 3A4 inhibitors (e.g., ketoconazole).			
Szonyi, 1995[73] RCT Country not reported N: 60	Outpatients of either sex aged over 70 with symptoms of urinary frequency, urgency and urge incontinence were recruited. Patients had to be mobile, able to attend an outpatient department, able to keep a diary chart and willing to give consent.	Urinary infections at the time of recruitment, patients with severe hepatic or renal disease, glaucoma, or uncontrolled diabetes. Patients on concomitant anticholinergic therapy with imipramine were excluded.	Oxybutynin 2.5 mg twice daily	Placebo	Funded by Smith and Nephew Pharmaceuticals Ltd.
Thuroff, 1991[74] Study: RCT N: 169	15 years old and older complaining of symptoms of frequency, urgency and/or incontinence, in whom cystometry findings were related to detrusor hyperactivity, whether idiopathic (unstable detrusor) or neurogenic (detrusor hyperreflexia) in origin.	Pregnancy, congestive heart failure, severe renal/liver disease, myasthenia gravis, unable to swallow/uncooperative patient, hiatal hernia/reflux esophagitis, gastrointestinal tract obstruction, urinary tract obstruction, residual urine greater than 50ml, untreated urinary tract infection and hyperreflexia without urge	Oxybutynin chloride	Propantheline and placebo	Pharmcia Leo Therapeutics, Helsingborg, Sweden provided the pharmaceutical preparations used in this study
Toglia, 2010[75] Study: Post-hoc Karram, 2009[39] VENUS N: 739	Patients aged ≥18 years with OAB symptoms for ≥3 months	Reported previously-18995887	Solifenacin	Placebo	Supported by Astellas Pharma US, Inc. and GlaxoSmithkline
U.S. Food and Drug Administration[76] Cardozo, 2008[77] Study: SUNRISE N: 865	Male of female aged ≥18 years, from whom written consent had been obtained, and who were willing and able to complete a voiding diary correctly; symptoms	NR	Solifenacin	Placebo	Research grant from Astellas Pharma Europe Ltd.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	of OAB (including urinary frequency, urgency or urgency incontinence) for ≥3 months and three or more episodes of urgency with or without incontinence in the last 3 days				
U.S. Food and Drug Administration, 2004[78] Study: RCT Sample: 680	Male and female subjects, aged 18 years and older with symptoms of overactive bladder for at least 6 months. Subjects must exhibit all of the following symptoms of overactive bladder during the run-in period: 1) incontinence 2) frequency of micturition -at least 8 times per 24 hours, on average, over the run-in period 3) urgency - at least once per 24 hours, on average, over the run-in period		Darifenacin	Placebo	NR
U.S. Food and Drug Administration, 2004[79] Study: RCT N: 562	Male and female subjects, aged 18 years and older with symptoms of overactive bladder for at least 6 months. Subjects must exhibit all of the following symptoms of overactive bladder during the run-in period: 1) incontinence 2)		Darifenacin	Placebo	NR

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	frequency of micturition -at least 8 times per 24 hours, on average, over the run-in period 3) urgency -at least once per 24 hours, on average, over the run-in period				
U.S. Food and Drug Administration, 2007[80] Study: RCT N: 601	Patients currently undergoing OAB therapy at the time of enrollment were required to undergo 7-day wash-out period, followed by 3-day baseline urinary diary collection, prior to randomization. Patients not under OAB therapy could begin treatment after 3-days of baseline diary collection	NR	Trospium chloride ER	Placebo	Indevus Pharmaceuticals, Inc.
U.S. Food and Drug Administration, 2007[81] Study: RCT N: 564	Patients currently undergoing OAB therapy at the time of enrollment were required to undergo 7-day wash-out period, followed by 3-day baseline urinary diary collection, prior to randomization. Patients not under OAB therapy could begin treatment after 3-days of baseline diary collection	NR	Trospium chloride ER	Placebo	Indevus Pharmaceuticals, Inc.
Chapple, 2005, 2007[82-84] U.S. Food and Drug Administration(905-EC-001)	The STAR study :men and women aged at least 18 years who	Stress incontinence or mixed incontinence where stress was predominant (mixed	Solifenacin 5 mg	Tolterodine ER 4 mg	Grant from Yamanouchi Pharmaceutical Co, Ltd

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
STAR study group Country: not reported N: 1,177	had OAB symptoms (including urinary frequency, urgency or urgency incontinence) for 3 months or more; with an average of >8 micturitions/day; >1 incontinence episode/day, or an average of >1 urgency episode/day.	incontinence was allowed otherwise) and patients with a neurological cause of abnormal detrusor activity.			(now Astellas Pharma Inc). Tokyo, Japan.
Vardy, 2009[85] Study: RCT VIBRANT Sample: 768	Eligible patients (aged ≥18 years) were required to have OAB symptoms for ≥3 months (≥8 micturitions and ≥1 urgency episode, with or without incontinence, per 24 hours) and a PPBC score ≥3	Significant stress or stress-predominant mixed incontinence, recurrent urinary tract infection (UTI; ≥3 episodes within the past 3 months) or evidence of UTI at baseline, evidence of chronic urologic inflammation/interstitial cystitis or urinary/gastric retention.	Solifenacin	Placebo	Research grant from Astellas Pharma U.S. Inc. and Glaxo-Smithkline
Wang, 2006[86] RCT Taiwan N: 74	Age: 16 to 80 years; OAB for more than 6 months. No patients had taken anticholinergics or tricyclic antidepressants and none had been treated with pelvic floor muscle training, bladder training, or pelvic prolapse repair.	Pregnancy, neurologic disorders, diabetes mellitus, demand cardiac pacemaker or intrauterine device use, genital prolapse greater than Stage II of the International Continence Society grading system, a postvoid residual urine volume greater than 100 mL, overt urinary stress incontinence, a history of any incontinence surgery, and urinary tract infection.	Electrical stimulation (ES)	Oxybutynin, placebo	Grant from National Science Council, Taiwan.
Yamaguchi, 2007 [87] Study: RCT N: 1593	Men and women aged ≥20 years and with symptoms of OAB reported for ≥6 months were eligible for screening and study enrolment. To	Significant BOO, an assessment based on measuring the postvoid residual urine volume(PVR); patients with a PVR of ≥100mL; presence of BOO symptoms assessed by	Solifenacin 5mg or 10mg	Propiverine or placebo	Funded and sponsored by Astellas Pharma Inc.(formerly Yamanouchi Pharmaceutical Co. Ltd), Tokyo, Japan

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
	be eligible for randomization after the 2-week placebo run-in period, patients had to report a mean number of voids/24 hr of ≥8, ≥3 episodes of urgency and/or ≥3 episodes of urgency incontinence during a 3-day voiding -diary period.	investigators(who were all urologists); urinary retention, demonstrable stress incontinence, bladder stones, UTI, interstitial cystitis, previous or current malignant disease of the pelvic organs; those taking concomitant anticholinergic medications; known hypersensitivity to anticholinergic medications or lactose.			
Zellner, 2009[88, 89] Study: RCT N: 1659	Male or female outpatients aged ≥18 years with urinary frequency ≥8 micturitions per day) and urge incontinence (≥5 episodes per week), as verified in the micturition diary.	Patients were excluded if they did not complete the micturition diary correctly for 7 consecutive days to confirm that they met the inclusion criteria and to establish baseline symptoms and urgency severity before the entrance visit. Based on this diary, patients with a total daily urine volume ≥2.8 L (determined by total daily urine for 2 days, divided by 2), a mean micturition volume of >250 mL, and/or a clinically significant bladder outlet obstruction (i.e., postvoid residual urine volume of >100 mL, determined via sonography) were also excluded as were those with an indwelling catheter or intermittent self-catheterization. Those with other significant medical problems or urogenital conditions, including urinary tract infection at the screening visit (or before or at the entrance visit), interstitial	Oxybutynin Hydrochloride	Trospium Chloride	Dr. R. Pfleger GmbH (Bamberg, Germany) sponsored this study. Petra Schwantes, PhD, Biomedical Services, assisted with the writing of this article; she received compensation from the sponsor.

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		cystitis and/or hematuria (as determined via urinalysis), contraindications to anticholinergic therapy (e.g., untreated narrow-angle glaucoma, mechanical gastrointestinal stenosis, myasthenia gravis syndrome), tachycardiac arrhythmia, severe psychiatric illnesses, or hypersensitivity to trospium chloride or oxybutynin or 1 of the vehicle ingredients, were also excluded. Patients who had participated in a bladder-training program, or in another study within 30 days before screening, were also prohibited, as were those undergoing electro stimulation programs. Further reasons for exclusion were alcohol and/or drug abuse, pregnancy, breastfeeding, and insufficient contraception among women of childbearing age.			
Zinner, 2005[90] RCT US N: 76	Males and non-pregnant (nor breastfeeding) females aged 18–85 years with urge incontinence (>4 significant incontinent episodes per week, where significant was defined as leakage that would normally require a change of clothing or absorbent pad) and urinary frequency (≥8 voids per day, on average).	Neurogenic bladder or stress incontinence, contraindications to antimuscarinic therapy, previous bladder or prostate surgery, bladder stones (as demonstrated by pelvic x-ray or ultrasound), acute or chronic urinary tract infection, significant urinary outflow obstruction, and clinically significant concomitant disease; Patients intending to start or modify either an existing bladder training program or existing treatment	Darifenacin controlled-release tablets 15 mg and 30 mg once/daily	Oxybutynin 5 mg three times daily, Placebo	Industry and grant

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		with thyroid or estrogen hormone replacement therapy; those who had received treatment with drugs that affect bladder function/urine production in the previous 2 weeks.			
Zinner, 2006[91] RCT Country not reported N: 445	Men and women aged >18 years with a history of OAB for >6 months and on average >1 urge incontinence episodes/day; >8 micturitions/day; >4 urgency episodes/day and mean warning time of <15 minutes during 12 consecutive hours.	Stress urinary incontinence; marked cystocele or pelvic prolapse; those taking the following drugs in the 2 weeks prior to the screening visit: anticholinergic/antispasmodic drugs, or those with anticholinergic effects, cholinergic agonists, potent cytochrome P450 3A4 inhibitors, opioids and drugs that cause significant constipation; those who have contraindications to anticholinergic drugs, clinically significant bladder outlet obstruction, have the intention to start a bladder training program and an indwelling catheter or intermittent self-catheterization.	Darifenacin 15 mg controlled release qd	Placebo	This study was funded by Novartis Pharma AG
Zinner, 2004[92] Trospium Study Group. USA N: 523	The Trospium Study Group: male and female 18 years or older with OAB symptoms for at least 6 months; with urinary urgency, a minimum voiding frequency of 70 voids per week with at least 7 urge incontinence episodes per week.	Predominantly stress UI , insensate or overflow in nature; with neurogenic bladder disorders, significant renal disease, uninvestigated hematuria and urinary tract infection at washout or more than twice during the prior year; significant bladder outlet obstruction (post-void residual volume >100 ml); concurrent use of any anticholinergic drug or other drug therapy for overactive bladder within 21	20 mg trospium twice daily	Placebo	Indevus Corporation

Randomized controlled clinical trials that examined drugs for urgency urinary incontinence (continued)

Reference Study, Sample	Inclusion Criteria	Exclusion Criteria	Active	Control	Sponsorship
		days before randomization, history of bladder surgery within 6 months before randomization, bladder cancer or interstitial cystitis were excluded from study; diuretic use, estrogen therapy and nonmedical bladder therapy that was not part of a stable, long-term program.			

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